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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/225,502	01/06/99	MOORE P	PF392

HM12/0322

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EXAMINER	
DECLOUX, A	
ART UNIT	**PAPER NUMBER**
1644	16

DATE MAILED: 03/22/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/225,502	Moore, P. et al
Examiner	**Group Art Unit**
DeCloux, Amy	1644

☒ Responsive to communication(s) filed on *delivered 1-10-01*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *21-56 and 58-103* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *21-56 and 58-103* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Detailed Action

1. Applicant's amendment, delivered 1-10-01(Paper No. 18), is acknowledged.

Claim 57 has been canceled. Claims 21-56 and 58-103 are currently pending.

2. In view of applicant's amendment delivered 1-10-01(Paper No. 18), the 112 second rejection is withdrawn as is the new matter rejection as applied to claims 52-103 as described in Section 8 of the previous office action mailed 10-27-99. However, the 101 and 112 first rejections are maintained.

3. Applicant traverses the objection to the specification made in the previous office action mailed 10-27-99, on the grounds that the recited passage to be inserted into the specification is from the priority document of Provisional application Number 60/070,875 which is hereby incorporated by reference on page 1, lines 4-6 of the instant specification. However, to incorporate material by reference, the host document / application must identify with detailed particularity what specific material it incorporates and clearly indicate where the material is found in the various documents. See Advanced Display Systems, Inc. v. Kent State Univ., 54 USPQ2d 1673 (Fed. Cir. 2000) citing In re Seversky, 177 USPQ 144, 146 (CCPa 1973). Since there is no direction to which section(s) of said provisional are to be incorporated, the new matter objection is maintained and repeated below for applicant's convenience, though applicant's arguments have been carefully considered.

4. The amendment filed 4-26-00 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the four paragraphs on the first and second pages of the amendment which was directed to be inserted at page 14, between lines 14 and 15 of the instant specification. There appears to be nothing incorporated by reference in the specification to support the added material.

Applicant is required to cancel the new matter in the reply to this Office action.

5. With regard to the 101 utility rejection, the examiner agrees with applicant that the specification asserts an immunosuppressant utility, however the examiner contends that this assertion is neither substantial nor well established, and disagrees with applicant's contention that the asserted immunosuppressive utilities for the novel FKBP-13 polypeptide of U.S. Patent 5,498,597 incorporated by reference, confers a specific and substantial utility to the proteins of the instantly recited nucleic acids.

Applicant contends that the specification discloses on page 6, lines 29-35 that the homology to FKBP65 suggests that the protein product would be useful for screening assays for the discovery of immunosuppressant drugs and in the treatment of diseases caused by overactive immune system. However the examiner notes that the first use is not a real world use, and the only support for the latter use is only supported in the instant specification by homology of the recited amino acid sequence to FKBP65. Furthermore the examiner notes that this overall homology of the recited amino acid sequences of SEQ ID NO:6 and SEQ ID NO:8 is less than 50% identical with FKBP65 with a BLAST search. The applicant has attached a paper by Galat et al as exhibit B, in which Galat teaches the structural features that contribute to the common activity of this family of proteins. However, this is no indication disclosed that the SEQ ID NO:6 and SEQ:ID NO:8 have the indicated structural features, nor is there disclosed any such biological activity.

In acknowledging the response to comment No. 19 in the Utility guidelines 66F.R. (No.4) at 1096, January 5, 2001, the examiner agrees with applicant that FK506 binding proteins are a class of useful proteins and assignment of a new protein to the class of sufficiently conserved proteins would impute the same specific substantial and credible utility to the assigned protein. However, as noted above there is insufficient guidance disclosed that would lead one to believe that the recited invention contains the well characterized properties of said class of proteins based on sequence homology alone. It is noted that the structural features that applicant contend contribute to the common activity of this family of proteins are exemplified in the applicant's attached paper by Galat The examiner further notes that though applicants believe that said paper is said to be incorporated by reference, it may fail to meet the requirements of incorporation as discussed in Section 3 which states to incorporate material by reference, the host document / application must identify with detailed particularity what specific material it incorporates and clearly indicate where the material is found in the various documents. See Advanced Display Systems, Inc. v. Kent State Univ., 54 USPQ2d 1673 (Fed. Cir. 2000) citing In re Seversky, 177 USPQ 144, 146 (CCPa 1973).

The examiner maintains the position that there is no specific disease or specific function disclosed for the recited nucleic acids, nor is there any substantial immunosuppressant function asserted other than that deduced from overall sequence homology. And the examiner disagrees with applicant's inference from said position that a protein is useful only if it can be used for only one disease, said inference was clearly not stated nor implied by the examiner.

The examiner maintains the position that said homology does not necessarily

place the protein encoded by the recited nucleic acid into the class that binds the FK506 class of immunosuppressant compounds, and does not agree with applicant's extension of this position as meaning either that being a member of a class of proteins renders a particular member of that class unpatentable, or that a protein's utility needs to be unique to only that protein in order to be sufficiently specific to be patentable. Said extension was clearly not stated nor implied by the examiner.

The examiner also maintains the position that the mapping of the recited nucleotide to a chromosomal location is an example of a non specific utility, which was one of several characteristics disclosed in the specification, none of which contributed to a specific, substantial utility. And the examiner disagrees with applicant's extension of said position being interpreted that an immunosuppressant-based utility is not sufficiently specific and not distinguishable from this mapping example. Said extension was clearly not stated nor implied by the examiner. The examiner does contend, as noted above, that the immunosuppressant-based utility asserted by applicant is not substantial with regard to the instant invention.

The examiner agrees with applicant that the utility is credible, but maintains the lack of a substantial, well established utility. Therefore, though applicant's arguments have been carefully considered, the rejection is maintained and is repeated below for applicant's convenience.

6. *35 U.S.C. § 101* reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, In such full, clear, concise, and exact terms as to enable any person skilled In the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 21-56 and 58-103 are rejected under 35 U.S.C. 101 because the claimed invention lacks a credible, substantial, specific, or well-established utility.

Claims 21-56 and 58-103 are drawn to polynucleotides encoding proteins that have homology to the FK506 binding protein FKBP65 and methods of expressing these proteins, the proteins of SEQ ID NO: 6 and 8, nucleotides and proteins having 95% homology to SEQ ID NO:s 5-8, heterologous nucleic acid and polypeptides, complement, secreted vector, host cell, method of producing the polypeptides and

pharmaceutical compositions thereof. The claimed polynucleotides and polypeptides are not supported by either a specific and substantial asserted utility or a well-established utility. The specification fails to provide objective evidence of any activity for the encoded proteins or to show that these proteins even exist. Applicant only states that the sequence has homology to the FK506 binding protein FKBP65. Therefore, SEQ ID Nos:5-8 have no well-established utility. A well-established utility is a specific, substantial, and credible utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. Identifying a polynucleotide as encoding a FKBP65-like protein does not endow the polynucleotide with such a utility. The instant specification discloses that FKBP65 is a FK506 binding protein and confers immunomodulating activity to FK506, rapamycin and cyclosporin A, (Page 6, lines 20-26 of the instant specification). Identifying a protein as having homology to FKBP65, does not indicate what function it and thus the encoding polynucleotide might have. There is no specific disease or specific function disclosed that is suggested by this homology; no disclosed conserved regions that would indicate that the claimed polypeptides function similarly to FKBP65 are identified in the instant specification. There is therefore no specific, substantial, or credible utility that is well-known, apparent, or implied by the relationship of the instant polynucleotide to the polynucleotide encoding a FKBP65-like protein or fragments thereof, nor the FKBP65-like protein or fragments thereof, nor the claimed heterologous versions of said proteins and nucleic acids, nor the claimed complement of said nucleic acids, nor the claimed pharmaceutical compositions thereof, nor the claimed homologs of said proteins and nucleic acids, nor the claimed methods of producing the claimed polypeptides.

The claimed polynucleotides also lack a specific or substantial utility. . The utilities identified by the applicant on beginning on page 22 are also not specific or substantial. A utility such as chromosome localization would apply to virtually every naturally occurring polynucleotide and is therefore not specific. Likewise, tissue-specific expression does not rely on specific properties or functions of the encoded protein, nor do uses including gene therapy, forensic uses and uses in molecular techniques such as Northern and Southern blots and antibody production. Further, the specification does not disclose any diseases or conditions known to be associated with the encoded protein, clearly further research would be required to identify a disease in which the encoded protein is involved and would be of significance; Therefore, the polynucleotide and the encoded polypeptide and derivatives thereof therefore lack a substantial utility. See Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966), noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." A patent is therefore not a license to experiment. See also the Revised Interim Utility Guidelines available at www.uspto.gov.

9. Applicants traverse the written description rejection on the basis that the federal circuit recently reemphasized that the description must clearly allow persons of ordinary

skill in the art to recognize what is claimed. First it is noted that there is no evidence disclosed that the proteins encoded by the DNA even exist. And therefore it is not clear what variants of said putative proteins sequences are encompassed by a genus. Further, though The applicant notes that the specification explicitly describes the genus of amino acid sequences having 95% identity to SEQ ID NO:s 6 and 8 and that therefore the skilled person could readily derive the claimed genus and that the structure of said genus is based on the 95% homology, it is not known which sequences confer an essential part of the homology since based on the 2 sequences any number of amino acid residues could potentially be absent. However since the 5% dishomology in terms of deletions, additions, and substitutions can occur anywhere along the protein, and the common structure to the genus is not disclosed in the instant specification, it is not clear which changes can be tolerated in the sequence of the instant polypeptides and still retain their putative immunosuppressive activity. And without a common structure, there is no genus and hence there is a lack of written description as in *Lilly* . Further applicants argue that Galat provides the structural basis for the genus but it is not clear where this is disclosed in the instant specification, and if the actual portion of this article is actually incorporated into the instant specification. Therefore, though applicant's arguments have been carefully considered, the rejection is maintained and repeated below for applicant's convenience.

10. Claims 38-51 and 68-80 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant has described the polynucleotide sequences consisting of SEQ ID NOs:5 and 7, as well as nucleotides encoding the amino acid sequence of SEQ ID NOs:6 and 8. However, the claims as written encompass polynucleotides that encode proteins with 95% homology to SEQ ID NO:s 6 and 8, that vary substantially in length and also in nucleotide composition. The instant disclosure of two nucleic acids, that of SEQ ID Nos:5 and 7, does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly&Co.*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

The specification discloses the isolated cDNA sequence SEQ ID NOs:5 and 7 and the translated amino acid sequence of SEQ ID NOs: 6 and 8. The specification does not provide evidence that the proteins of SEQ ID Nos:6 and 8 actually exist. There is no description of the required structural and functional features of said proteins, or of the conserved regions that would be critical for these features. Further,

the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify the polynucleotides encompassed.

Therefore, applicant has not disclosed sufficient species such that one skilled in the art would conclude that applicant was in possession of the claimed genus of polynucleotides encoding polypeptides 95% identical to SEQ ID NOs: 6 or 8.

Therefore, the structure of these elements is not conventional in the art and one of skill in the art would not recognize from the disclosure that applicant was in possession of the genus of nucleic acids, including genes, encompassed by the claimed invention.

11. With regard to the enablement, applicant traverse based on the grounds that the skilled person could readily make nucleic acid molecules encoding polypeptides with 95% identity to SEQ ID Nos: 6 and 8, with which the examiner agrees. However, the examiner disagrees with applicant's contention that skilled person could use said nucleic acid that encode the polypeptides with 95% identity to SEQ ID Nos: 6 and 8 since it is not clear which sequence changes can be tolerated and still retain the function of the polypeptides having the amino acid sequence of SEQ ID No:6 and SEQ ID NO:8, especially when the function of said polypeptides has not been established and there is no disclosure that said sequences have the structural features of the family of FK506 binding proteins taught by Galat (exhibit B by applicant) nor is any indication in the instant specification that said polypeptides possess the PPIase activity of immunophillins as taught by Galat, or any other properties of FK506 binding protein. Therefore, though applicant's arguments have been carefully considered, they are not deemed persuasive and the rejection is maintained and repeated below for applicant's convenience.

12. Claims 38-51 and 68-80 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 38-51 and 68-80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for nucleic acid molecule encoding SEQ ID NO:6, and SEQ ID NO:8, does not reasonably provide enablement for a nucleic acid molecule comprising a nucleotide sequence encoding an amino acid sequence at least 95% identical with residues of SEQ ID NO:6 and SEQ ID NO:8, nor with nucleic acid molecules comprising heterologous sequences, recombinant vector, recombinant host cell, a method of producing said polypeptide, or a composition of said nucleic acid molecule.

Additionally, the specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Factors to be considered in determining whether undue experimentation is required are summarized In *In re Wands* (858iF2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, unpredictability in the art, the amount of experimentation required, and the amount of direction or guidance presented.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation. Besides the polynucleotides encoding polypeptides with the sequences SEQ ID NO:6, and SEQ ID NO:8, respectively, the specification fails to provide guidance as to how to make or use the claimed polynucleotide encoding a polynucleotide with at least an 95% identity to the claimed sequences. Since the nucleic acid sequence of a polynucleotide determines its protein coding properties, predictability of which changes can be tolerated in a polynucleotide's nucleic acid sequence and still retain similar functions and properties requires a knowledge of, and guidance with regard to which nucleic acids in the nucleotide sequence, if any are tolerant of modification and which are conserved (ie., expectedly intolerant to modification), and detailed knowledge of the ways in which the product's structure relates to its functional usefulness. However, the problem of predicting functional aspects of the product from mere sequence data of a single nucleic acid sequence and what changes can be tolerated is complex and well outside the realm of routine experimentation. *In re Fisher*, 1666 USPQ 19 24 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Without such guidance, the fragments which can be made and used to encode peptides of the claimed activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly extensive and undue. See *Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

Therefore, the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of nucleic acid encoding the amino acid sequences broadly encompassed by the claims due to the significant number of untaught sequences. Therefore, there is no evidence of record to show that one skilled In the art would be able to practice the invention as claimed without an undue amount of experimentation.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance In the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

13. No claim is allowed.

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy DeCloux whose telephone number is (703) 306-5821. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 pm. a message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located In Crystal Mall 1. The faxing of such papers must conform with the notice published In the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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March 26, 2001

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